

## (12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization  
International Bureau(43) International Publication Date  
23 October 2003 (23.10.2003)

PCT

(10) International Publication Number  
WO 03/087038 A1(51) International Patent Classification<sup>7</sup>: C07C 233/63, (74) Agent: GROS, Florent; Novartis AG, Corporate Intellectual Property, CH-4002 Basel (CH).  
231/22

(21) International Application Number: PCT/EP03/03864

(22) International Filing Date: 14 April 2003 (14.04.2003)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:  
60/372,625 15 April 2002 (15.04.2002) US

(71) Applicant (for all designated States except AT, US): NOVARTIS AG [CH/CH]; Lichtstrasse 35, CH-4056 Basel (CH).

(71) Applicant (for AT only): NOVARTIS PHARMA GMBH [AT/AT]; Brunner Strasse 59, A-1230 Vienna (AT).

(72) Inventor; and

(75) Inventor/Applicant (for US only): SUTTON, Paul, Allen [US/US]; 34 Irvington Road, Parsippany, NJ 07054 (US).

(81) Designated States (national): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LT, LU, LV, MA, MD, MK, MN, MX, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SE, SG, SK, TJ, TM, TN, TR, TT, UA, US, UZ, VC, VN, YU, ZA, ZW.

(84) Designated States (regional): Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR).

## Published:

- with international search report
- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: CRYSTAL FORMS OF N-(TRANS-4-ISOPROPYLCYCLOHEXYLCARBONYL)-D-PHENYLALANINE

(57) Abstract: New crystal forms of N-(trans-4-isopropylcyclohexylcarbonyl)-D-phenylalanine, also known as nateglinide, may be produced by dissolving nateglinide in any of its forms, including solvates, in an organic solvent to form a solution followed by precipitation of nateglinide from the solution, and isolating and drying the precipitated crystal form of nateglinide. The precipitation of nateglinide may be induced either by cooling the solution, or by addition of another solvent which is miscible with the first solvent but in which nateglinide is only poorly soluble, or by combination of the two. Depending on the solvent a specific crystal form of nateglinide may be obtained, e.g., the R'-type crystal form of nateglinide produced by the described method has a different melting point, infra red spectra and X-ray diffraction patterns from the previously known crystal forms of nateglinide.

WO 03/087038 A1

## INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP 03/03864

A. CLASSIFICATION OF SUBJECT MATTER  
IPC 7 C07C233/63 C07C231/22

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07C

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

CHEM ABS Data, WPI Data, EPO-Internal, PAJ

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 5 463 116 A (M. SUMIKAWA ET AL) 31 October 1995 (1995-10-31) cited in the application the whole document	1,2
A	----- DATABASE CAPLUS 'Online! CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; retrieved from STN Database accession no. 2001:625224 XP002249976 abstract & G. LI ET AL: YAOXUE XUEBAO, vol. 36, no. 7, 2001, pages 532-534,	1
P,A	----- WO 03 022251 A (ALEMBIC LTD) 20 March 2003 (2003-03-20) the whole document	1,2



Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

## \* Special categories of cited documents:

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
- \*E\* earlier document but published on or after the international filing date
- \*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- \*O\* document referring to an oral disclosure, use, exhibition or other means
- \*P\* document published prior to the international filing date but later than the priority date claimed

- \*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- \*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- \*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
- \*G\* document member of the same patent family

Date of the actual completion of the international search

4 August 2003

Date of mailing of the international search report

25/08/2003

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2  
NL - 2280 HV Rijswijk  
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  
Fax: (+31-70) 340-3016

Authorized officer

Van Amsterdam, L

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/EP 03/03864

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
US 5463116	A	31-10-1995	CA 2114678 A1	02-08-1995
			US 5488150 A	30-01-1996
			AT 149483 T	15-03-1997
			DE 69217762 D1	10-04-1997
			DE 69217762 T2	09-10-1997
			EP 0526171 A2	03-02-1993
			ES 2100291 T3	16-06-1997
			JP 2508949 B2	19-06-1996
			JP 5208943 A	20-08-1993
			LU 90843 A9	04-02-2002
			LU 90846 A9	04-02-2002
			BR 1100807 A3	28-12-1999
			DK 526171 T3	25-08-1997
WO 03022251	A	20-03-2003	WO 03022251 A1	20-03-2003